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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/063,584	05/03/2002	Audrey Goddard	10466/351	2701

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EXAMINER	
HUNNICUTT, RACHEL KAPUST	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 12/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/063,584	EATON ET AL.	
	Examiner	Art Unit	
	Rachel K. Hunnicutt	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 November 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1104*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RESPONSE TO AMENDMENT

Applicant's amendment filed November 5, 2004 is acknowledged. Claim 6 has been canceled. Claim 1 has been amended. Claims 1-5 are pending and under consideration. The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior office action.

Claim Rejections/Objections Withdrawn

The objection to the specification regarding the use of trademarks is withdrawn in response to Applicant's amendments to the specification.

The rejection of claim 6 under 35 U.S.C. 101 as not be supported by either a specific and substantial asserted utility or a well-established utility is withdrawn in response to Applicants' cancellation of the claim.

The rejection of claim 6 under 35 U.S.C. 112, second paragraph, is withdrawn in response to Applicants' cancellation of the claim.

The rejection of claim 6 under 35 U.S.C. 112, first paragraph, for lack of enablement due to the invention not being supported by a specific or substantial asserted utility or a well-established utility, is withdrawn in response to Applicants' cancellation of the claim.

The rejection of claims 1-5 under 35 U.S.C. 103(a) as being unpatentable over Fujikawa-Adachi et al. is withdrawn in response to Applicants' arguments on p. 14-15 of the response. The rejection of claim 6 under 35 U.S.C. 103(a) as being unpatentable over Fujikawa-Adachi et al. is withdrawn in response to Applicants' cancellation of the claim.

Claim Objections/Rejections Maintained

Claim Rejections - 35 USC § 101

The rejection of claims 1-5 under 35 U.S.C. 101 is maintained for reasons of record on p. 3-4 of the office action of paper no. 0704.

Applicants argue that the PRO1335 polypeptide is differentially expressed in certain cancers compared to normal tissue and is useful as a diagnostic tool. Applicants refer to Example 18 which shows that mRNA for PRO1335 is more highly expressed in normal stomach, lung, rectal, and skin tissue compared to stomach, lung, rectal, and melanoma tumor tissues. One declaration of J. Christopher Grimaldi (Exhibit 1) teaches that the DNA libraries used in the gene expression studies were made from pooled samples of normal and of tumor tissues. Grimaldi states in section 6 that "I conducted a semi-quantitative analysis of the expression of the DNA sequences of interest in normal versus tumor tissues. Expression levels were graded according to a scale of +, -, and +/- to indicate the amount of the specific signal detected. Using the widely accepted technique of PCR, it was determined whether the polynucleotides tested were more highly expressed, less expressed, or whether expression remained the same in tumor tissue as compared to its normal counterpart. Because this technique relies on the visual detection of ethidium bromide staining of PCR products on agarose gels, it is reasonable to assume that any detectable differences seen between two samples will represent at least a two fold difference in cDNA."

Furthermore, in another declaration of J. Christopher Grimaldi (Exhibit 2), Grimaldi states that when a gene is overexpressed, the gene product or polypeptide will also be overexpressed (p. 10 of response). The declaration of Dr. Paul Polakis avers that mRNA levels typically correlate with an increase in abundance of the encoded protein (p. 10 of response). Applicants further cite Orntoft *et al.*, Hyman *et al.*, and Pollack *et al.* in support of the argument that in the vast majority of cases, the combined teachings of the art teach that gene amplification influences gene expression and that gene expression influences protein levels. In addition, Applicants refer to the declaration of Dr. Ashkenazi and cited references Hanna and Mornin who teach that even if higher levels of mRNA do not correlate with an increase in abundance of the encoded protein, that type of information is also useful in diagnosing and treating patients.

Applicants' arguments have been fully considered but have not been found to be persuasive. A utility of being a diagnostic target for stomach, lung, rectal, or melanoma tumors is a utility that requires or constitutes carrying out further research to identify or reasonably confirm a "real world" context of use. This is not a substantial utility. In Example 18, the specification merely states that the gene is "more highly expressed" in one tissue as compared to another. There is no guidance in the specification as to how high the levels are. The declaration of Grimaldi (Exhibit 1) does not teach the level of reproducibility or the level of reliability of the results. Neither the specification nor the declarations provide any evidence that indicates what the differences were or whether the results were statistically significant. Applicants have provided no indication of the nature or number of samples that were used. In addition, one cannot determine from the data in the specification whether the observed "amplification" of nucleic acid is due to increase in chromosomal copy number, or alternatively due to an increase in transcription rates. The only thing Applicants teach is that the gene was "more highly expressed", and this does not enable the skilled artisan to differentiate amongst expression levels in order to diagnose any diseases.

At paragraph 4 of the second Grimaldi declaration (Exhibit 2), the declarant discusses mutations of Her2/Neu, and chromosomal translocations that are known to be associated with cancer, and states that "If the chromosomal aberration results in the aberrant expression of a mRNA and the corresponding gene product (the polypeptide) as they do in the aforementioned cases, then the gene product is a promising target for cancer therapy, for example, by the therapeutic antibody approach." This argument has been fully considered but is not deemed persuasive because it evinces that the instant specification provides a mere invitation to experiment, and not a readily available utility. The PRO1335 gene, unlike Her2/Neu, has *not* been associated with tumor formation or the development of cancer, nor has it been shown to be predictive of such. Similarly, unlike t(5;14), no translocation of PRO1335 is known to occur. All that the specification demonstrates is that the PRO1335 nucleic acid was more highly expressed in normal stomach, lung, rectal, and skin tissue compared to stomach, lung, rectal, and melanoma tumor tissues. No mutation or translocation of PRO1335 has been associated with stomach, lung, rectal, or skin cancer. In the absence of any of the above information, all that the specification does is present evidence that the DNA encoding PRO1335 is amplified in an

unknown number of samples, and invite the artisan to determine the rest of the story. Such is insufficient to meet the requirements of 35 U.S.C. §101 for the claimed antibodies.

Whether or not increased levels of PRO1335 mRNA correlate with increased levels of PRO1335 protein is not an issue. The declarations and cited references do not establish a substantial utility for the PRO1335 nucleic acid molecules. As stated above, the specification does not provide sufficient guidance to the skilled artisan to diagnose or treat any disease. Thus, there would be no specific utility for antibodies which bind to PRO1335 proteins.

Claim Rejections - 35 USC § 112

The rejection of claims 1-5 under 35 U.S.C. 112, first paragraph, for lack of enablement due to the invention not being supported by a specific or substantial asserted utility or a well-established utility, is maintained for reasons of record on p. 5 of paper no. 0704.

Conclusion

NO CLAIMS ARE ALLOWED.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rachel K. Hunnicutt whose telephone number is (571) 272-0886. The examiner can normally be reached on Mon-Fri 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

RKH
12/23/04